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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,042	08/28/2001	Mark A. Conkling	5051.471	4291

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	20

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,042	CONKLING ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *33-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16,11* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *IDS 1 1/2* .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-32) in Paper No. 19, filed 19 May 2003is acknowledged. The traversal is on the ground(s) that a search of these groups would overlap with a search on group I and thus examination of all groups would no be an undue burden to the Office. This is not found persuasive because none of the methods of Groups II-IV are drawn to use of the promoter of SEQ ID NO:1. Thus, a search of all groups would not be coextensive.

The requirement is still deemed proper and is therefore made FINAL. Claims 33-73 are withdrawn from consideration as being drawn to nonelected inventions.

2. The abstract is not descriptive of the instant invention, which is drawn to a nucleic acid comprising a Nic gene product responsive element, plants transformed with it and a method of reducing the level of nicotine in a tobacco plan. Also, in the abstract the abbreviation "TSNA" is not defined. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

3. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

Claim Objections

4. Claims 4, 8, 11-13, 18 and 22-32 are objected to because of the following informalities:

The article before "DNA" in claims 4, 18 and 29 should be deleted.

In claim 8, the second recitation of "microparticle" in line 2 is misspelled.

Claim 8 has two periods at the end of the claim.

In claim 11, line 6, --wherein-- should be inserted before "said" and "containing" should be replaced with -- comprise s--.

In claims 12-13, line 1, --wherein-- should be inserted after the comma and "containing" should be replaced with --have-- in claim 12, and with --comprise-- in claim 13.

There is an improper article before "tobacco" in claims 22-23 and 30-32.

In claim 24, line 1, --wherein-- should be inserted before "said" and in line 2, "containing" should be replaced with --comprise--.

In claim 25, line 2, --is-- is missing from before "selected".

Claims 25-29 start with an improper article.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid of SEQ ID NO:1, does not reasonably provide enablement for 20-455 nucleotide fragments of SEQ ID NO:1 or nucleic acids that hybridize to SEQ ID NO:1 and that are "responsive to" a *Nic* gene product, methods of using the nucleic acid to reduce the levels of nicotine in a tobacco plant, and plants thereby produced. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to 20-455 nucleotide fragments of SEQ ID NO:1 or nucleic acids that hybridize to SEQ ID NO:1 and that are "responsive to" a *Nic* gene product, methods of using the nucleic acid to reduce the levels of nicotine in a tobacco plant, and plants thereby produced.

The instant specification, however, only provides guidance for characterization of the minimal sequence for the NtQPT1 promoter by deletion analysis to show that the -586 to -2000 region produced the highest expression levels of GUS (example 1); transformation of the deletion constructs into *nic*$^-$/ *nic*$^-$ tobacco plants and crossing to produce *Nic*$^+$/ *nic*$^-$ and *nic*$^-$/ *nic*$^-$ progeny with the construct at the same locus to show that *Nic* gene products bound between -1000 and -600 or -700 bp of the NtQPT1 promoter (example 2); prophetic transformation of the region between -1000 and -600 or -700 bp of the NtQPT1 promoter or tandem arrays of that region into produce plants with reduced nicotine levels (examples 3 and 6-7).

The instant specification fails to provide guidance for 20-455 nucleotide fragments of SEQ ID NO:1 or nucleic acids that hybridize to SEQ ID NO:1 and that are "responsive to" a *Nic* gene product, methods of using the nucleic acid to reduce the levels of nicotine in a tobacco plant, and plants thereby produced.

The instant specification fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NO:1, wherein the nucleic acid is responsive to a *Nic* gene product. The specification fails to teach *Nic* gene product responsive elements from other plants.

It is not clear that the binding site of the *Nic* gene product is between -1000 and -600 to -700 of the NtQPT1 promoter. The data in Table 3 show that the drop in GUS production between -1300 and -1000 is about the same as that between -1000 and -600 to -700.

The specification does not teach which parts, particularly which 20 nucleotide long fragments, of the region between -1000 and -600 to -700 of the NtQPT1 promoter is that to which the *Nic* gene product binds. Which 20-455 nucleotide fragments reduce the level of nicotine in a plant and do so without negatively affecting other functions in the plant?

Use of molecular decoys has only been done using short dsDNAs transiently transfected into cells (see, e.g., Morishita et al, 1998, Circulation Res. 82:1023-1028, paragraph spanning pg 1023-1024 and paragraph spanning the columns on pg 1026). Transformation of a plant with a molecular decoy, wherein the decoy is present is integrated in multiple copies in the plant genome, has not been done. The instant specification fails to provide guidance for how many copies of the *Nic* gene product responsive element are required to reduce the levels of nicotine in tobacco.

The specification fails to teach transformation of a tobacco plant with a linear construct or the integration into the plant genome of a short dsDNA transfected into a plant. Note that integration of such construct is necessary for regeneration of a transformed cell into a whole plant that has reduced levels of nicotine and for production of seed that can produce such a plant. Claim 28 claims a tobacco plant comprising a circular construct. The specification fails to teach autonomously replicating circular recombinant constructs for plant transformation.

As the specification does not teach any tobacco plant transformed with Nic responsive elements, undue trial and error experimentation would be required to screen through the myriad

of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with reduced nicotine levels, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled for 20-455 nucleotide fragments of SEQ ID NO:1 or nucleic acids that hybridize to SEQ ID NO:1 and that are "responsive to" a *Nic* gene product, methods of using the nucleic acid to reduce the levels of nicotine in a tobacco plant, and plants thereby produced.

7. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that comprise 20-455 nucleotide fragments of SEQ ID NO:1 or that hybridize to SEQ ID NO:1, wherein the DNA molecule is a *Nic* gene product responsive element from any source. In contrast, the specification only describes the region between -1000 and -600 or -700 bp of the NtQPT1 promoter; where this is located on SEQ ID NO:1 is unclear. It is also unclear if the region is sufficient to reduce the amount of nicotine in a plant. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that that comprise 20-455 nucleotide fragments of SEQ ID NO:1 or that hybridize to SEQ ID NO:1, wherein the DNA molecule is a *Nic* gene product responsive element and wherein the DNA molecule is sufficient

to reduce the amount of nicotine in a plant, within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1, 14 and 25 are indefinite in their recitation of "acids" in parts (a) and (b). Does a *Nic* gene product responsive element comprise numerous nucleic acids, and if so, how many?

Claims 1, 14 and 25 are indefinite in their recitation of "responsive to a *Nic* gene product" in part (b). It is unclear what is means for a nucleic acid to be responsive to a *Nic* gene product. What does it do to "respond" to it? If the *Nic* gene product binds to the nucleic acid, it is the *Nic* gene product that responds to the nucleic acid - the nucleic acid itself does not do anything to "respond" to the gene product.

Claims 1, 14 and 25, part a, and claim 2, line 3, are indefinite in their recitation of "wherein said fragment is between 20-455 consecutive nucleotides". It this its length? Is this where it is located on SEQ ID NO:1?

Claim 5 is indefinite in its recitation of "isolated nucleic acid according to claim 1,further comprising a recombinant nucleic acid construct". The claim should be rewritten to claim a recombinant nucleic acid construct comprising the nucleic acid of claim 1. As currently written, it is not clear if the nucleic acid is part of the recombinant nucleic acid construct or merely attached to it; thus, for example, it is not clear in claim 9 if the nucleic acid is part of the vector. In claim 7 it is not clear if the nucleic acid is part of the circular construct or if the circular construct has the nucleic acid attached to in some manner. Claims 16-17 and 27-28 have similar problems - for example, the nucleic acid is both within a construct and joined to the construct?

Claim 8 should be rewritten to claim a microparticle, wherein the microparticle is coated with the nucleic acid of claim 1. See also claim 11 of US Patent 5,837,876.

Claim 12 lacks antecedent basis for the limitation "said tobacco leaves" in line 2.

Claim 13, line 4, is indefinite in its recitation of "regenerated". Plants are not regenerated form seeds, because seeds were never plants to begin with. Plants are grown from seeds.

Claim 16 lacks antecedent basis for the limitation "said isolated nucleic acid" in line 2

Claims 23 and 32 are indefinite because it is not clear if the tobacco seed comprises the Nic gene product responsive element. Not all progeny seed will comprise the nucleic acid with which their parent as transformed.

Claim 24 is indefinite in its recitation of "exogenous" in line 2 and claims 27 and 29 are indefinite for the word in line 1. *Nic* gene product responsive elements are tobacco nucleic acids, so it is not clear how these nucleic acids could be exogenous to the tobacco plant.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Conkling et al (WO 97/05261).

Conkling et al teach a nucleic acid comprising SEQ ID NO:1 or fragments thereof, including a fragment (del0.7) that comprises 148 nucleotides of SEQ ID NO:1 (see sequence search report) and a microparticle carrying the nucleic acid. Conkling et al also teach constructs comprising the nucleic acid operatively linked to the GUS gene and tobacco plants transformed

with them via *Agrobacterium* -mediated transformation (pg 19-22 and Figure 3). The nucleic acid would be linear in the transformed plants.

Note that MPEP 2111.03 states "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising.'"

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 16-22 of U.S. Patent No. 5,837,876. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because SEQ ID NO:1, as claimed in the issued patent, is identical to SEQ ID NO:1, claimed in the instant application. Additionally, SEQ ID NO:6, claimed in the issued patent, .comprises 148 nucleotides of SEQ ID NO:1 and would be a fragment of SEQ ID NO:1, claimed in the instant application. The constructs and vectors comprising SEQ ID NO:1 and 6 operatively linked to a coding sequence would be constructs and vectors comprising SEQ ID NO:1 and fragments thereof, as claimed in the instant application, and plants and cells transformed with the constructs and vectors via *Agrobacterium*-mediated transformation, as claimed in the issued patent, would be plants transformed with them via *Agrobacterium* - mediated transformation, as claimed in the instant application.

14. Claims 11-32 are free of the prior art, given the failure of the prior art to teach or suggest a method of reducing the level of nicotine in a tobacco plant by transformation with a Nic responsive element, and plants thereby obtained.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
July 25, 2003